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Weifan Zhang

Rebecca Liu

Chris Chatwin

Abstract

Medical device regulations across the globe have significant variations. The Chinese medical device market, like China's economy, is developing rapidly. This article reviews the medical device regulations in China and illustrates the major changes that have been recently implemented according to the new medical device regulations that came into force on the 1st June, 2014. Most regulatory research has focused on the US and EU medical device regulations with little written about the Chinese medical device regulations. The purpose of this article is to bridge the research gap and to introduce the Chinese medical devices regulatory environment to investors or companies who are engaged in the medical device market or doing business in China.

Keywords

Medical device, regulation, China, medical device market, regulatory frameworks

1. Introduction

“Medical Devices” — covers a very broad area, from simple but essential products (such as a wheelchair) to complex high-tech products (such as a pacemaker). Unlike ordinary products, medical devices utilise a large number of the latest achievements of modern science and technology and play a significant role in promoting human health. Due to the potential health risks, and the evaluation of the safety and effectiveness of medical devices, many countries have established medical device regulations for their supervision and management. Medical devices must be qualified by passing the safety and effectiveness procedures before they can be marketed in any particular country.

The US was the first country to legally define a ‘medical device’, and also was the first country to establish a medical devices management procedure.¹ As the second largest medical devices manufacturers and consumers in the world, the EU also has a rich history of medical devices regulation. The US and EU have established relatively mature medical device regulations, which have a key influence in the world. For instance, most of the guidance documents of the Global Harmonization Task Force (GHTF)ⁱ are based on the US and the EU medical device regulations. China established ‘Regulations for the Supervision and Administration of Medical Devices’ in 2000; these regulations aim to strengthen the supervision and administration of medical devices, ensuring their safety and protecting human health and life. The Chinese State Council released new Regulations for the Supervision and Administration of Medical Devices and these came into force on June 1st, 2014. The revisions are intended to create a more scientific and efficient regulatory regime for medical device supervision. There is little research into the Chinese medical device regulations because compared with the relatively mature US and EU regulations, Chinese regulations are evolving with the new regulations just released, hence there is a requirement for more research in this area. In this article, we describe the differences between the “Old Regulations” and the “New Regulations” to bridge the research gap. Generally speaking, the New Regulations moderate the supervision on low-risk devices and strengthens the oversight of high-risk devices. Thus, this article bridges the research gap and contributes to the Chinese medical device regulations area.

2. Medical Device Regulation in China

In the year of 1938, the US congress passed the Federal Food, Drug, and Cosmetic Act (the Act). The Act made provisions for medical devices. The US Food and Drug Administration (FDA) has the primary authority to oversee and manage medical devices, to make sure that the manufacturers produce safe and effective medical equipment.

Until the 1990s, in the area of medical devices, the EU enacted three directives to replace each member state’s regulations. The directives harmonised the EU medical devices market, ensuring medical device safety and a high level of protection for human health and effective functioning of the “single market”.

Relatively speaking, the Chinese medical device regulations were established late. In 2000, “Regulations for the Supervision and Administration of Medical Devices” were established, the regulations laid down the legal status of medical devices’ supervision and management. This was a milestone in China’s medical device regulation history. The “Regulations” gave the China Food and Drug Administration (CFDA) authority to oversee medical devices and ensure their safety and effectiveness, and protect human health and life.

ⁱ The organization GHTF (was born in 1992) has been permanently replaced by the International Medical Device Regulators Forum (IMDRF) in 2011.

China's definition for medical devices can be found in the Regulations for the Supervision and Administration of Medical Devices, 2000.² Medical devices are defined as:

Any instrument, apparatus, material, or other article whether used alone or in combination, including the software necessary for its proper application. It does not achieve its principal action in or on the human body by means of pharmacology, immunology or metabolism, but which may be assisted in its function by such means; the use of which is to achieve the following intended objectives:

1. Diagnosis, prevention, monitoring, treatment or alleviation of disease;
2. Diagnosis, monitoring, treatment, alleviation of or compensation for injuries or handicap conditions;
3. Investigation, replacement or modification for anatomy or a physiological process;
4. Control of conception.

Similar to the US medical devices regulation, the CFDA classify medical devices into three classes.² Class I devices are those for which safety and effectiveness can be ensured subject to routine administration (general controls) and do not need clinical trials; Class II devices need further controls (special controls) to ensure their safety and effectiveness. Class III devices are subject to strict controls because these kinds of devices may be implanted into the human body, or be for life support, they have the potential to put the patient's life at risk. For example: artificial heart valves or artificial kidney. The Chinese medical device registration system is different from the US system and EU system. In China, Class I devices are inspected and approved by the city's CFDA (city level). The province's CFDA (province level) are responsible for Class II devices' inspection and registration certificate. All the Class III devices are controlled by the State Council CFDA/central CFDA (national level).³ Most Class I devices can be registered for production directly but must follow general controls. Class II and III devices' registration is not only subject to special and strict controls, but also requires clinical trial evaluation before they are put into production. Furthermore, when importing medical devices into the Chinese market for the first time, no matter what the class level is, the central CFDA will be responsible for the device's supervision and administration. The importer needs to provide details of the devices' intended use, quality standards, testing methods, product sample and other relevant documents for the central CFDA oversight.

The US FDA has established classifications for about 1,700 distinct types of medical devices and organized them into 16 medical specialty "panels" such as cardiovascular devices or ear and nose devices. These panels can be found in 21 CFR Part 862-892.^{4, 5} These actions ensure that all the devices on the US market have scientific and unique names. The Class I and Class II devices accounted for 90% of medical devices in the US market, from which 47% of medical devices fall under Class I and 43% fall under Class II. 10% of medical devices fall under Class III (see Table 1). In addition, about 95% of Class I devices and a small number of Class II devices (about 8%) are exempt from the premarket notification process.⁶

Table 1. Percentage breakdown of medical devices classification levels.

Country/Class	Class I devices	Class II devices	Class III devices
US	47%	43%	10%
China	36%	41%	23%

The Chinese medical device classification criteria are similar to the US's. The CFDA classify the devices into three classes, see Table 1. There are no more than 5,000 types of medical devices in the Chinese market, but there are more than 60,000 devices that have the registration certificate issued by the CFDA regulatory agencies.⁷ The reason for this is that under the old standard, the naming of devices was inconsistent, this results in the same products having different names or the same names may be different products. In contrast, in the US, one device can only have one name

and one product code; different products have different names and codes. The US FDA device classification system is a database system associated with an expert group providing technical support; the EU devices classification system is based on the ‘Directives Rules’. The CFDA uses the devices ‘classification rules’ and ‘classification catalogues’ to implement the medical devices classification. For instance, when a device needs to be classified, the reviewers will first look for classification catalogues, if the product does not appear in the catalogues, the reviewers will classify the device according to the ‘classification rules’. In addition, only about 8%-10% of medical devices are classified as high-risk devices in the US whereas more than 20% of devices are classified as high-risk devices in China, see Table 1. For instance, the computed tomography (CT) scanner was classified into Class II devices in the US,^{8, 9} while it is classified into Class III in China.¹⁰ Too many products are classified as high-risk devices in China. This not only brings a heavy economic burden to the manufacturers, but also creates high cost and low efficiency for the government management. The US FDA pays more attention to review 10% high-risk Class III devices because they are usually the new products using new technology; In China, Class III devices accounted for 23% of the total devices, but, high-risk and innovative products do not exceed 5% of total applications for registration.¹¹

The Chinese medical device registration system is a hierarchical system, see Figure 1. This system theoretically should have a short processing time and high efficiency but can be slow. The CFDA has local regulatory agencies, which includes 31 provincial, 433 municipal and 1,936 county-level agencies. Technical organizations include 16 state, 122 provincial, 373 municipal and 436 county-level organizations.¹² The regulatory agencies (except county-level), can issue medical device registration certificates.

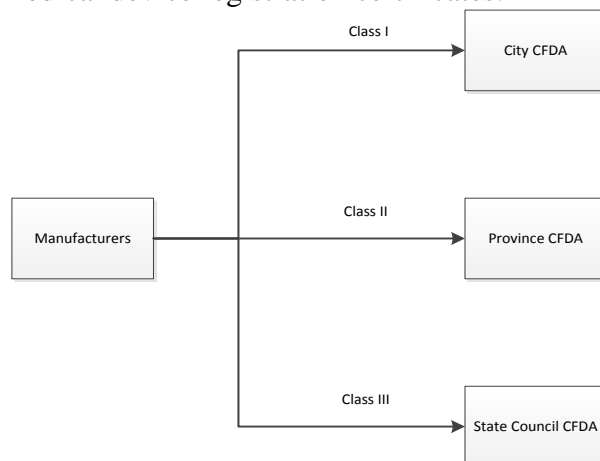


Figure 1 CFDA registration system

Medical devices in China are covered by China National Standards (GB standards) and professional/industry standards (YY standards).¹³ Medical devices must at least meet the requirements of the Chinese GB standards or professional standards, or meet other standards like ISO or equivalent if the devices want to sell in the Chinese market. Some medical devices still need the China Compulsory Certification (CCC) mark for product safety, such as medical diagnostic X-ray equipment, electrocardiograph, pacemaker, etc.¹⁴

China established the adverse events monitoring system and information networks, medical devices re-evaluation and medical device recalls but these systems are still under construction and need more legislative support.

The mission of the CFDA is: public health protection and to ensure that all the marketed medical devices are safe and effective. The CFDA usually carries out random testing for medical devices' manufacturers and users. The CFDA has established the adverse events systems to collect all the information on medical devices surveillance, this encourages medical devices related people to report any medical devices relevant information, like quality issues and serious injuries or deaths of patients.¹⁵

3. The New Medical Device Regulation in China—Major Changes

The Chinese State Council released the new Regulations for the Supervision and Administration of Medical Devices in 2014. Compared with the old regulations (48 articles), the new ones have 80 articles and many changes on device registration; clinical trials; adverse events; recalls, etc. The new regulations are consistent with the goal of the “National 12th five-Year Plan”ⁱⁱ to foster innovation and encourage domestic companies' research and development while enhancing the protection of public health.¹⁶ The government overhauls the regulations in order to catch up with the fast development in the medical device industry and economy.

According to the New Regulations, the revised definition of medical devices are:¹⁷

Any instrument, apparatus, appliance, in-vitro diagnostic reagent and calibrator, material, or other articles alike, including the necessary software, directly or indirectly used on human body, which functions by means of physical ways, instead of by means of pharmacology, immunology or metabolism, or the participation of pharmacology, immunology or metabolism means only plays an assistive role; the use of medical devices is to achieve the following expected purposes:

1. Diagnosis, prevention, monitoring, treatment or alleviation of disease;
2. Diagnosis, monitoring, treatment, alleviation of or compensation for injuries or handicap conditions;
3. Investigation, replacement, modification or support of a physiological structure or process;
4. Supporting or maintaining of life;
5. Control of conception;
6. Providing information for treatment or diagnosis purpose by inspecting the samples from human body.

3.1. Classification of Medical Device

The New Regulations classify and administer medical devices based on their risk levels. Class I medical devices are those with a low-risk level, which through routine administration their safety and effectiveness can be ensured; Class II medical devices are those with a middle-risk level, for which strict control and administration is required to ensure their safety and effectiveness; Class III medical devices are those with a higher-risk level, for which special measures and strict control shall be taken to ensure their safety and effectiveness. Compared with the old regulations, the new regime introduces risk management into the regulations. Risk management not only in the device classification sections, but also in other parts. For example, “medical device registration should submit a risk analysis report of the product; medical device recalls and adverse events”.

3.2. Medical Device Registration

According to the New Regulations, Class I devices will no longer require registration, but will change to record-filing. The applicant shall submit the required documents to a city level regulatory authority (same as the Old Regulations) for device record-filing procedure. The applicant shall submit the following material to the regulatory authority for Class I devices record-

ⁱⁱ Five-Year Plan (FYP) is a series of social and economic development initiatives, which renews every five years. The Five-Year Plan was shaped by the Communist Party of China, who plays a leading role in mapping strategies for China's economic development, setting growth targets and launching reforms. First FYP: 1953-1957, the rest can be done in the same manner. So 11th FYP is from 2006-2010 and 12th FYP is from 2011-2015.

filing and Class II and Class III devices registration: (1) Risk analysis report of the product; (2) Technical requirements of the product; (3) Testing report of the product; (4) Clinical trial material; (5) Product instructions for use and sample label; (6) Quality management system documentations related to research and development (R&D) and manufacturing of the product; (7) Other documents which prove the safety and effectiveness of the product. Moreover, the applicant for the medical devices record-filing or registration shall be responsible for the authenticity of the submitted documents.¹⁸ Like the Old Regulations registration procedure, Class II devices are administered by a provincial regulatory authority and Class III devices are administered by the central CFDA. Class I devices do not require clinical trials for the record-filing procedure, Class II and Class III devices require clinical trials for registration. However, clinical trials can be exempted in any of the following circumstances: the device is at least as safe and effective as a previously cleared (predicate) device (legally Chinese marketed device), which has similar intended use and no severe adverse events record; a medical device which proves to be safe and effective through non-clinical evaluation assessments; a medical device which proves to be safe and effective through the analysis and evaluation of the data obtained from clinical trials or clinical application of the substantially equivalent medical devices. In addition, the duration of the medical device registration certificate is five years (the Old Regulations suggest the registration certificate must be renewed every four years).

3.3. Medical Device Production

The New Regulations pay more attention to Good Manufacturing Practices (GMPs) for medical device production management. GMP is that part of quality assurance, which ensures that medical products are consistently produced to the required product specification and controlled to the quality standards appropriate to their intended use. GMP is concerned with both production and quality control.¹⁹

CFDA requires that all the medical devices in the Chinese market should be accompanied with product specifications and labels. In addition, the New Regulations require Class II and Class III devices should also indicate the registration certificate number and register's affiliations with product specifications and labels. Moreover, if the medical device can be used by the consumer independently, the product specifications and labels should include special instructions for its safe use.

According to the New Regulations, if a medical device is within a manufacturing consignment, the consigner shall be responsible for the quality of medical devices. The consignee shall be a medical device manufacturer which meets the CFDA's requirements. In addition, the imbedded medical devices with a high-risk level shall not be manufactured in consignments.²⁰

3.4. Distribution/Operation and Use of Medical Devices

The Old Regulations required companies who distribute/operate Class I medical devices to file records with the provincial CFDA. Companies distributing/operating Class II and Class III medical devices need to obtain the Medical Device Distributing Enterprise License, which is issued by the provincial CFDA. The New Regulations removes record-filing for Class I device distributors and requires Class II device distributors to file records with the provincial CFDA.

The New Regulations also place more obligations on medical device distributors and users. Such obligations cover all aspects of using medical devices including device supplier's certificates, quality certificates, records of purchase/sales, transportation and storage, operator technical

training. Moreover, the medical device user shall inspect, verify and maintain the devices periodically to ensure the devices are in good condition, safe and effective.

Imported medical devices shall be accompanied with product specifications or user manuals and labels in Chinese, and specify the devices' place of origin and agent's affiliations. The medical device exporters shall ensure the exported devices comply with the requirements of the importing countries.

3.5. Medical Device Adverse Events and Recalls

The Old Regulations were silent about medical device adverse events and recalls. However, the central CFDA and the Chinese Ministry of Health (MOH) issued provisional Decree 425 for tracking adverse events²¹ and provisional Decree 82 for managing medical device recalls²² in 2011, respectively.

The New Regulations issued requirements on monitoring medical device adverse events and managing recalls. These requirements set clear responsibilities from device manufacturer personnel to distributors and patients/consumers. The central CFDA established the medical device adverse events monitoring system and information networks to: collect information, analyse, evaluate and control adverse events in a timely manner. Any medical device manufacturer, distributor and user has rights to report adverse events to this monitoring system and information networks, and the CFDA will also collect adverse events information proactively.

The New Regulations require the device manufacturer to stop production if the device does not meet the compulsory standards or contains other defects, furthermore, they must notify relevant distributors or users to stop distributing or using this kind of device and recall the devices which are already on the market. According to MOH Decree 82, there are three levels of recalls based on the severity of medical device defects.²² Level I recalls means that if use of the medical device has caused, or may cause, serious health hazards that are of a permanent nature; Level II recalls means use of the medical device may cause health hazards that are of a temporary or permanent nature; Level III recalls mean use of the medical device may not be likely to cause harm but it is still defective.¹⁴

3.6. Supervision and Inspection

The New Regulations require that the CFDA enhance supervision and inspection of medical devices' registration, record-filing, production, distribution and use, sometimes using random checks. The provincial CFDA or central CFDA will issue medical device quality circulars based on the results of timely random checks.

The central CFDA has established a shared medical device supervision and inspection information network. The CFDA should legally and in a timely manner publish the medical devices' license, record-filing, random check results and illegal behaviour through the information network. In addition, the CFDA also established the credit files for medical device registrants, record-filing applicants, manufacturers, distributors and users, and increased the frequency of inspection upon those who have a poor credibility record. Moreover, the CFDA publish their contact information for inquires, complaints and reports. Information disclosure is a major breakthrough for the Chinese medical device market participants' supervision and inspection.

3.7. Legal Liabilities

The New Regulations have increased sanctions and penalties for various violations. For example, administrative penalties up to 20 times (5 times in the Old Regulations) the value of the

manufactured products may be imposed on medical devices produced without the proper permits. In some severe circumstances, relevant personnel and companies will be suspended from application for any medical device permits or licences for 5 years, and may be subject to criminal sanctions if such violation constitutes a criminal offense. Penalties or criminal offenses may be incurred for the following actions: permits (medical device registration certificate, production permit, distribution permit, advertisement approval certificate) are obtained by providing false information or by using other methods of cheating; relevant medical device permits or certificates are forged, altered, transferred, leased and lent; manufacture, distribute or use of devices which are not compliant with the compulsory standards or technical requirements; any clinical trials conducted in violation of the Regulations or medical device clinical trial institutes issuing false reports, etc.

4. Discussion

The New Regulations are intended to establish a more efficient and scientific regulatory regime for supervision and administration of medical devices. Risk management has been introduced to the New Regulations such as device classification. In addition, the CFDA pays more attention to the Class III devices supervision and moderates the Class I devices oversight. The Old Regulations required that all the Class II and Class III devices need clinical trials, inspection and approval by the provincial CFDA and central CFDA, respectively.³ The exemption from clinical trials for some special circumstances has been introduced in the New Regulations. Moreover, the registration certificate is replaced by record-filing for Class I devices application, which make the registration process more efficient.

As previously described, due to there not being a national unified product naming and coding system; too many devices are classified as high-risk devices when they should not be categorised at the high-risk level, resulting in an unnecessary waste of effort and low efficiency of medical device supervision in China. Nevertheless, the New Regulations have tried to establish a unique unified national medical device naming and coding system, to reduce the number of: “the same products having different names or the same names referring to different products”, and the central CFDA will analyse and evaluate medical device’s risk, to adjust the “classification catalogue”.²³

In the US and EU, the legislation clearly prescribes that the device manufacturer or applicant will take the main responsibilities for device safety and all the consequences resulting from the device performance. However, the old legislation did not clearly define this situation, the CFDA bears some responsibility for the medical devices’ use, failures, and even adverse events. The New Regulations clearly delineate every medical device related participant’s responsibilities. For example, medical device manufacturers, distributors and users shall monitor adverse events. If any adverse events are identified, they shall report it to the medical device adverse event monitoring technique institutes.²⁴

The post-market surveillance is an important guarantee to ensure that the devices continue to be safe and effective. The US and EU’s medical devices regulatory legislation have strict requirements for the marketed devices. For example, the EU has the vigilance system for post-market surveillance, such as the European Databank on Medical Devices (EUDAMED)ⁱⁱⁱ. The adverse events and recall of medical devices does not appear in the Old Regulations. The New

ⁱⁱⁱ EUDAMED contains data on manufacturers, authorized representatives and devices; certificates issued, modified, supplemented, suspended, withdrawn or refused; clinical investigations, which use is obligatory since May 2011. The purpose of EUDAMED is to enhance market surveillance and transparency in the medical devices area by providing Competent Authorities with quick access to information as well as to contribute to a uniform application of the Directive.

Regulations combined the central CFDA Decree 425 and MOH Decree 82 requirements, they clearly describe the device participants' responsibilities and have established the medical device adverse events monitoring system and information networks to control adverse events and recalls; they have established a re-evaluation system for registered medical devices to regulate supervisory activities.

5. Conclusions

The changes made in the New Regulations demonstrate the Chinese government's efforts to upgrade and maintain an effective regulatory framework for the medical device market. The Chinese government has promulgated the New Regulations, which covers various perspectives of the regulatory regime of medical devices, such as device classification and registration, supervision of production and distribution, etc. Driven by the more powerful regulatory requirements under the New Regulations, the Chinese medical device market will become increasingly dynamic in the future.

Further in-depth research on this topic will be carried out in the future. Some regulations and policies still need modification and the recommendation is for more studies to understand the changing market environments, this should result in continuous improvement of policies.

Declaration of Conflicting Interests

The authors declare that there is no conflict of interest

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